2

A Case for Government-Sponsored Monitoring of Preimplantation Genetic Diagnosis in the United States

Aaron D. Levine

Preimplantation genetic diagnosis (PGD), a modified version of in vitro fertilization in which individual embryos are screened for specific genetic characteristics prior to implantation, provides a powerful way for parents suffering from infertility to increase their chances of having healthy children. In its various forms, PGD allows parents to screen for gender, providing a means for avoiding X-linked diseases, chromosomal abnormalities, such as translocations and aneuploidies, and single-gene disorders. Beyond these standard uses, PGD could potentially be used to select for any genetic trait, and this aspect of the technology has raised concerns that it may be used either intentionally or unintentionally for eugenic purposes. At present, reproductive medicine is only loosely regulated in the United States and new technologies, such as PGD, are almost entirely unregulated. This paper argues that given the lack of consensus regarding the ethical acceptability of PGD and embryo selection techniques, the government has an interest in gathering and reporting data on the use of PGD in the United States. Taking a proactive role now, rather than allowing the use of PGD to continue growing unscrutinized, will give society the chance to make thoughtful and deliberate decisions about its use.[1]

Aaron D. Levine is a Ph.D. candidate in Public Affairs at the Woodrow Wilson School of Public and International Affairs, Princeton University (adlevine@princeton.edu).

Introduction

The ethics of assisted reproductive technologies (ART) have been the subject of public debate at least since the late 1970s, when in vitro fertilization (IVF) revolutionized the field. Although today IVF is almost universally accepted as a means to help parents suffering from various forms of infertility to reproduce, newer forms of ART continue to generate widespread controversy. This paper focuses on the technology of preimplantation genetic diagnosis (PGD), a variant of IVF in which embryos are selected for implantation based on specific genetic characteristics of interest. ART, including PGD, are loosely regulated in the United States, in keeping with the tradition of reproductive freedom. This article argues that, given the ethical debate currently surrounding PGD and other embryo selection techniques, the government has an interest in at least minimal regulation of PGD for the purpose of monitoring its use. A minor modification to the Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA) is likely to be the most politically expedient way to introduce this necessary regulation.

This paper is divided into three sections. The first part reviews the field of reproductive medicine up to the development of PGD in 1990. I then consider the uses of PGD during its brief history and possible uses of the technology in the future. Part two reviews some of the major ethical concerns regarding PGD. These include concerns related to the destruction of human embryos and unequal access to treatment, which also apply to more mainstream reproductive technologies, such as IVF, as well as concerns specific to PGD related to the potential eugenic and discriminatory consequences of selection. The third section outlines current policies governing the use of ART in the United States today. I also examine the FCSRCA and consider the possibility of modifying this regulation to include additional technologies, such as PGD.

Reproductive Medicine: Past, Present, and Future

A Brief History of Reproductive Medicine

Reproductive medicine, the field of medicine concerned with the treatment of infertility, has a lengthy history. The first reported case of artificial insemination, known today as artificial insemination by donor (AID), took place in 1884, but the procedure was only rarely used until the 1950s when techniques for the long-term preservation of sperm were developed (Henig 2004). In the late 1980s, more than 170,000 couples in the United States

used AID each year. The technique is almost certainly more common today although no accurate statistics are available (Critser 1998).

The modern field of reproductive medicine took shape when Louise Brown was born through the use of IVF technology in 1978 (Steptoe and Edwards 1978). IVF requires several steps (Braude and Rowell 2003): (1) extraction of oocytes from the woman, (2) fertilization of these oocytes by sperm, (3) culture of the resulting embryo(s) for several days, and (4) transfer of some of these embryos into the woman's uterus. Each of these steps involves numerous complications depending on the source(s) of infertility, and the basic technique has been modified in a variety of ways to handle more difficult cases.

The oocyte extraction process takes place following a cycle of hormonal stimulation, which leads a woman to release more mature eggs than normal. Retrieving these mature eggs has traditionally required laparoscopic surgery under general anesthesia, with all of the side effects of a typical surgical procedure, but recently a less invasive alternative has become the method of choice (Braude and Rowell 2003).

In the early years of IVF, fertilization was a simple process that involved adding semen to the oocytes in a petri dish. However, this process has been modified to handle cases where infertility derives either completely or in part from the male. In the case of defective sperm, a technique known as intracytoplasmic sperm injection (ICSI) is utilized (Braude and Rowell 2003). In this method, as the name suggests, a single spermatozoa is injected directly into the oocyte.

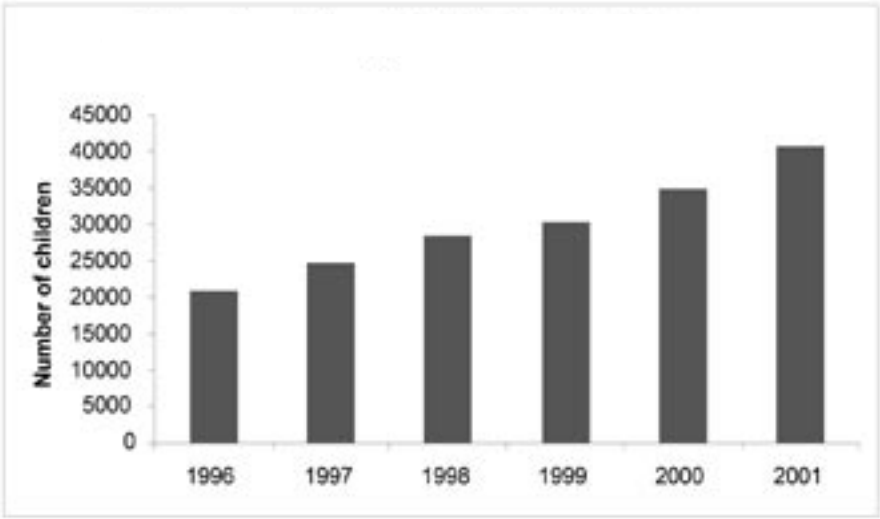
Following fertilization of the extracted oocyte, the embryo is allowed to grow *in vitro* for several days prior to implantation. During this period, healthy embryos normally divide several times and reach the six to eight cell stage. Only embryos that seem to be dividing normally and appear healthy to visual inspection are transferred to the woman's uterus. More recently, new techniques have allowed clinicians to grow human embryos in culture for up to five days, allowing the embryos to reach the blastocyst stage (Gardner, Lane and Schoolcraft 2000). Although it has not yet been confirmed, clinicians hope that culturing embryos to this later stage will improve implantation rates following transfer.

Transfer of the embryo from the petri dish into the mother's womb has proven to be a particularly difficult step to control. Ideally, clinicians would like to transfer one embryo, but low success rates have made this impractical, leading to more typical transfer rates of two to four embryos per IVF cycle. These higher rates lead to a greater number of pregnancies, but have the unfortunate side effect of greatly increasing the number of

multiple birth pregnancies. Multiple births stress the public health system and are associated with increased risk for both mothers and infants. These risks include an increased likelihood of premature delivery, low birth weight and long-term disability among infants (Wright et al. 2003).

The use of IVF in the United States has grown dramatically since its introduction in 1981, and the Centers for Disease Control and Prevention (CDC) estimate that the technology now accounts for roughly 1 percent of births in the United States (U.S. Department of Health and Human Services 2003). CDC data show that the number of IVF births has increased from approximately 20,000 in 1996 to roughly 40,000 in 2001 (Figure 1). Interestingly, in the United Kingdom, where IVF is much more closely regulated by the government, the technology also accounts for roughly 1 percent of total births (U.K Office of National Statistics 2003; HFEA 2002).

Figure 1: Number of Children Born through the Use of IVF Technology in the United States



Source: CDC Annual ART Reports, compiled by author.

Current Uses of Preimplantation Genetic Diagnosis (PGD)

PGD was developed in 1990 for two primary reasons (Handyside et al. 1992). The first was to enable parents with a high likelihood of conceiving children with genetic disorders to greatly reduce this risk. The second was to increase the success rate of IVF in difficult cases. The theory behind this second rationale was that one of the major sources of failure in IVF is the transfer of defective embryos, which then failed to implant properly or spontaneously aborted early in the pregnancy.

The technique of PGD is closely related to that of IVF. The only difference is the addition of a screening step during the culturing of the embryos prior to the transfer into the woman's uterus. In a typical case, embryos will be allowed to mature in culture until they reach the six to eight cell stage. At this point a small hole is made in the protective covering surrounding each embryo and one or two cells are extracted. This process is referred to as an embryo biopsy. The technique used to screen the extracted cells depends on the goal of the PGD. A technique known as polymerase chain reaction (PCR) is typically utilized to screen for single gene disorders, while fluorescence in situ hybridization (FISH) is used to screen for chromosomal abnormalities. Only embryos that pass the relevant screening test are considered for transfer to the woman's uterus.

Today PGD has three main uses (Braude et al. 2002; Sermon 2002). The first of these uses is screening for single-gene disorders. PGD was first demonstrated as a technique to screen for cystic fibrosis, one of the most common genetic disorders in the United States, and in the ensuing years the technique has been expanded to many other diseases. The European Society for Human Reproduction and Embryology (ESHRE) PGD consortium, a group of approximately twenty-five reproductive medicine centers that provide PGD, has published a partial list of single-gene disorders for which they have screened (Table 1) (ESHRE PGD Consortium Steering Committee 2002). This list almost certainly contains the diseases screened for in the majority of this type of PGD procedure, but should not be considered exhaustive.

Table 1: Single Gene Disorder Indications for PGD in 2001

	Dominant	Recessive
Autosomal	Central core disease Charcot-Marie-Tooth 1A Charcot-Marie-Tooth 2A Crouzon syndrome FAP-Gardner HD-exclusion Huntington's disease* Marfan's syndrome Myotonic dystrophy* Neurofibromatosis Osteogenesis imperfecta I Osteogenesis imperfecta IV Stickler syndrome Tuberous sclerosis	Beta-thalassaemia* CDG1C Cystic fibrosis* Epidermolysis bullosa Gaucher's disease Hyperinsulinaemic hypoglycaemia PHH1 Sickle cell Soubak muscular atrophy Tay-Sachs disease
Sex-linked	Alport syndrome Fragile X syndrome* Oro-facial-digital syndrome type I	Agammaglobulinaemia Alport syndrome Duchenne's muscular dystrophy* Hunter's syndrome MPSII Spinal and bulbar muscular atrophy

** Denotes most common indications by inheritance mode.*
Source: ESHRE PGD Consortium Steering Committee 2002.

The other two uses of PGD both relate to screening for chromosomal abnormalities as opposed to single-gene disorders. Screening is currently possible for both numerical and structural abnormalities. Numerical abnormalities, in which embryos have the wrong number of chromosomes, are known as aneuploidies. Most aneuploidies are fatal, but some lead to viable offspring. The most common aneuploidy in humans is Down syndrome, which occurs when a person has three copies of chromosome twenty-one in each cell. PGD for aneuploidy screening is used primarily for high risk IVF patients, such as older women (greater than thirty-five years) or for couples who have experienced recurrent IVF failure. Aneuploidy screening has been the fastest growing use of PGD in the ESHRE data set in recent years (ESHRE PGD Consortium Steering Committee 2002).

PGD is also used to screen for structural chromosomal abnormalities, known as translocations. Translocations occur when chromosomes break and then rejoin other chromosomes. In some cases this process results in the translocation carrier retaining a full complement of genetic material but having significantly reduced fertility because many of his or her gametes

contain the incorrect amount of genetic material. In the case of patients with recurrent IVF failure, PGD using FISH technology can be used to identify embryos that have a full complement of genetic material and thus are much less likely to spontaneously abort.

Little data exists on the prevalence of PGD worldwide. The ESHRE does provide a tabulation of PGD births by its member clinics and this is the most widely cited source, but it is certainly not complete. They report roughly 250 children born through PGD between 1999 and 2001. Another measure of the prevalence of PGD is the number of clinics performing the technique. Although no accurate measure exists in the United States, in the United Kingdom nine of the seventy-two IVF clinics were licensed to perform PGD in 2002, although only five centers reported actually performing the procedure between 1997 and 2001(HFEA 2002; U.K. Department of Health 2002).

Possible Future Uses of Preimplantation Genetic Diagnosis

Today PGD is used almost exclusively to screen for single-gene disorders or chromosomal abnormalities, but it is not difficult to imagine more controversial uses of the technology. Lee Silver, in his book *Remaking Eden,* imagines a world in which parents choose between numerous embryos, each ranked on a whole host of genetic characteristics (Silver 1997). Parents could consider not only whether or not their future child would be afflicted with any single-gene disorders, but also their predisposition to a variety of more complex diseases with both genetic and environmental components, such as heart disease and cancer. Parents, in Silver's scenario, could even select the "physiological and physical characteristics" of their future child.

The designer child scenario presented in *Remaking Eden* sounded like science fiction when it was first published in 1997, and still does today in many regards. However, it is clear that biology is moving rapidly in a direction that could make this vision a reality. Following the completion of the human genome sequence (International Human Genome Sequencing Consortium 2004) and the rapid advancement in DNA microarray technology, which permits high speed genome-wide screening, the number of technological leaps required to make the designer child scenario a reality is rapidly shrinking.

Still, several key technological hurdles must be surmounted before PGD could be used in such a dramatic manner. The first of these is the limited number of eggs available. Most current oocyte extraction procedures yield roughly a dozen eggs, although sometimes twice this many are retrieved

(Melie et al. 2003). Many more than this would be necessary to give parents ample choice. To illustrate this point, imagine that a couple was hoping to select for a specific allele at just four genes. If the parents were heterozygous at each of the four genes and wanted a child homozygous for a particular allele for each gene, this desired combination would only result, on average, in one out of every 256 embryos.

Assuming this hurdle could be overcome, it would then be necessary to efficiently screen these embryos for all of the genetic traits of interest and create some sort of genetic profile based on this screening. Although DNA microarrays could potentially be used to screen the embryos quite rapidly, the limited amount of genetic material available in the small number of cells biopsied could be a critical issue. And if this limitation was overcome, it would still be necessary to somehow turn this data into a coherent and meaningful genetic profile.

Finally, once all of these hurdles were overcome, the success rate of the transfer step in IVF would need to improve. Currently only a small percentage of embryos transferred into women's uteruses implant properly and give rise to children. This percentage would need to increase significantly for the technology of designer children through PGD to gain widespread use.

While none of these problems have trivial solutions, they are by no means insurmountable. Given the historical rate of progress in biomedical research, it does not seem unreasonable to predict that many, if not all, of these technological hurdles will be overcome in the not-too-distant future. Still, those who argue that such a scenario could only take place several years into the future are certainly correct. However, the mere fact that a scenario is not imminent does not mean it should not be considered. Furthermore, in its most recent survey the ESHRE found for the first time use of PGD for social as opposed to medical purposes (ESHRE PGD Consortium Steering Committee 2002). Although this social use was one of the simplest selections imaginable, selecting for gender, the very fact that it occurs today with such limited technology suggests that social use of PGD might become more prevalent as the technology grows more powerful.

Although it is impossible to predict how this field will develop, it seems plausible to hypothesize that PGD or some similar form of genetic selection will become widely available in the future. And once such a technology is available, it seems almost certain that some people would want to use it. The size of this group is unclear, but the technology would certainly have the potential to gain in popularity rapidly and this might result in

a situation where a sizable percentage of parents were using it. Parents in the United States already spend thousands of dollars on private education, saxophone lessons and countless other environmental enhancements for their children. In many ways selecting what they view to be the best genes for their children is a natural extension of this behavior.

Ethical Considerations

Destruction of Human Embryos

One of the benefits touted by early proponents of PGD was its ability to reduce the need for parents to choose abortion. Before PGD, parents who were carriers of a recessive disease could not determine if their child would have the disease until several months into the pregnancy through the use of prenatal screening techniques, such as chorionic villus sampling or amniocentesis. Parents might then be forced to decide between abortion and raising a child afflicted with a serious genetic ailment. PGD allows parents to make the decision prior to the implantation of the embryo, which theoretically allows the decision to be made with less difficulty.

Despite many viewing this as a benefit of PGD, the technology remains ethically controversial because it leads to the discarding of human embryos. For those who believe that an early embryo is a person and should be granted full moral status equivalent to any other person, such deliberate creation and destruction of embryos is morally problematic. These concerns lead some to conclude that PGD is morally unacceptable.

In the United States, strong differences persist in individual views on the moral status of human embryos. A workable, though controversial, compromise based on the Supreme Court's decision in *Roe v. Wade* has cleared the way for abortion up to the point of viability and clearly places PGD within the bounds of legality at the current time.

Equal Access

Another important ethical concern regarding PGD relates to access to the technology. At the present time, PGD is an expensive add-on to an expensive procedure and is rarely, at least in the United States, covered by insurance. This means that the benefits of PGD are disproportionately available to the wealthy. In the United States, unequal access to technology is the norm, and this situation is not typically treated with much concern. However, if PGD becomes more prevalent and access issues persist, the level of concern may increase. This type of concern falls into the general category of distributive justice.

As long as PGD remains a fringe technology used by a few thousand

parents to improve their chances of having a healthy child, distributive justice concerns will most likely be of little significance. But in a hypothetical future where 20 percent of the parents in the United States chose to use PGD in order to select a genetic profile for their children, access to the technology would become increasingly important. If the technology remained available only to the wealthy, the concept of equal opportunity, so important to citizens of the United States, might be violated. Furthermore, if PGD gave the children of the rich a significant advantage, it could easily be seen as perpetuating class differences and over time, some have argued, even lead to a permanent schism between classes (Kitcher 2003).

Many distributive justice concerns can be sidestepped as ethical issues if one imagines the government as a provider of basic levels of key services. Although these sorts of programs are relatively rare in the United States, both Medicare and Social Security provide precedents that could be followed.

Enhancement

Many people who are comfortable with the use of PGD to screen for single gene disorders are troubled when the technology is utilized for nonmedical purposes. This medical/nonmedical distinction is clear in some cases. For example, many people would distinguish between PGD for Tay-Sachs disease and PGD to select eye or hair color. In their eyes, using PGD to screen for Tay-Sachs or cystic fibrosis serves a clear medical need and, thus, should be allowed. On the other hand, using PGD to screen for eye or hair color is not medically indicated and should be prohibited.

Yet, despite the ease with which this distinction is applied in simple cases, borderline cases are significantly harder to adjudicate. Should screening for genes that impact obesity or height be considered medical treatments and thus allowed, or are they outside the boundaries of medicine? What about genes impacting sexual orientation, if such genes could be found?

The answers to these questions vary dramatically by individual and eventually come down to one's definition of health and of the goal of health care. Two major views are present in the literature: one posits that the aim of health care is to correct deficiencies and thus bring everyone to some norm of health (Daniels 1998); the other views the goal of health care as bringing each individual closer to optimal functioning (Stock 2002).

These two views have widely divergent consequences. The first view supports treatment for disease but lends little support to the use of PGD to influence other traits, such as height, weight, or intelligence. The critical issue with this type of definition is how one defines the norm to which everyone is entitled. The issue of medical treatment to increase height il-

lustrates the difficulties with this process. In the United States, treatment with human growth hormone (HGH) has become an accepted approach to treat children who suffer from low HGH levels. This qualifies as treatment of a deficiency and is supported by the first definition. However, many children with normal levels of HGH are the same height as children with the HGH deficiency. Is it appropriate to treat these children with HGH as well? According to the first definition, the answer would be no. Yet this situation would leave non-HGH deficient, but nonetheless short, patients at a disadvantage in a society where being tall confers clear advantages (Steckel 1995).

These kinds of complexities have led some to embrace the more inclusive second definition of health. This broad definition includes essentially any treatment that seems to have the ability to improve an individual. Thus any short child would be a candidate for HGH treatment. However, tall children would be candidates as well. In fact, as long as you could make a case that it would be better to be taller, this second definition of health care would support your treatment with HGH.

This inclusive definition of healthcare includes many forms of PGD, as it potentially covers selection for alleles that affect characteristics ranging from intelligence to muscular endurance to bone density. However, it is not all inclusive. Some traits, such as eye color, remain that have no medical benefit no matter how broad the definition. Many of these traits seem trivial and some would argue that society need not concern itself with their selection. However, others would argue that it is their very triviality that suggests they should not be the target of a technology, such as PGD, which has as its inevitable byproduct the destruction of human embryos.

Currently, there is widespread disagreement in the United States regarding the acceptability of the use of PGD for enhancement. Most Americans approve of PGD for clear medical uses but disapprove of its use to select a child's gender or other desirable characteristics. However, a significant minority (20 to 30 percent) approves of these practices (Genetics and Public Policy Center 2002). Bioethicists and policy analysts are similarly divided. Some feel the technology is a natural extension of already acceptable enhancements and need not be a source of undue concern (Pence 2000). Others feel that, while it may be problematic initially, it is inevitable and likely beneficial in the long-run (Silver 1997). Still others see it as a disastrous practice which moves procreation from the bedroom to the laboratory and accelerates the process of commoditizing children (Kass 2002). As these divergent views illustrate, thoughtful and reasonable people can disagree on an important issue related to PGD. Many of

these disagreements occur at fundamental levels and it seems unlikely that consensus will be reached in the near future.

Eugenics

Eugenics is defined as the improvement of the human race through selective breeding, and recalls stories of coercive practices in the United States through the first half of the 20th century and, even more vividly, the atrocities of Nazi Germany in World War II (Paul 1995). Yet while the days of governmental control of reproduction are in the past, in the United States at least, some believe that PGD ushers back in a much more insidious new form of eugenics.

This fear is based on a vision of many different parents choosing similar traits for their children. Over time, as PGD gained prevalence, children would become increasingly similar genetically. Although there is no reason to think that parents would choose identical traits for their children, it is not difficult to imagine a group of desirable traits being selected by the majority of parents. This possibility becomes particularly conceivable when one considers the influence of external forces, such as the media, in determining personal preferences in U.S. society. The extent of such a homogenization effect is hard to predict and may or may not be important, but it would be largely unprecedented in human history and must be cause for some concern.

To estimate the possible extent of homogenization in the United States, consider the following hypothetical scenario. Suppose that a particular allele was randomly distributed among all Americans with a frequency of 50 percent. That is, this particular allele made up half of all the alleles at that locus in the American gene pool. Now, suppose a scientist discovered that this particular allele, when in the homozygous state, was highly correlated with a generally undesirable but common trait, such as obesity. Many Americans might decide to use PGD to select children lacking this allele. If, for example, 20 percent of parents chose to use PGD, the percentage of children in the next generation that were homozygous for the allele would decrease from 25 percent to 20 percent. If 20 percent of the next generation used PGD for the same purpose, the percentage would drop to 16 percent. This represents a decrease in the frequency of the allele in the entire population from 50 percent to 44 percent. This small drop in overall frequency is due to the fact that selection against the homozygous state often leads to de facto selection for heterozygous carriers. In contrast, if 20 percent of parents chose to use PGD to select against both the homozygous and heterozygous states, the overall frequency of the allele would fall from 50 percent to 32 percent in two generations. Lower levels

of selection over many generations could have similar effects.

One concern with homogenization is that it might pose a danger to the future of the human race. As almost every high school biology student learns, variation is the driving force behind natural selection. A significant reduction in genetic diversity could potentially reduce humanity's ability to cope with new and unforeseen circumstances.

Supporters of PGD argue that we have already irrevocably altered natural selection though advanced medical care and thus need not be concerned about possible dangers posed by homogenization. However, the impact society has had on the human gene pool thus far is minor compared with the potential impact of widespread selective reproduction, and there is certainly no consensus that following such a policy would be wise.

Another concern is that this homogenization could occur despite limited knowledge about the complex role various genes play. If preliminary knowledge suggested that a particular allele was detrimental to short-term memory, for instance, it might rapidly be selected against. Many years could pass before the allele's important role in controlling cholesterol or hand-eye coordination or some other trait was fully understood. In this case, the selection would be to the detriment of the individuals born through PGD.

Some scholars attempt to counter this concern by suggesting that we would eventually find a way to replace the allele we had mistakenly rejected. However, this replacement may be nontrivial. While PGD is a technology that is relatively well-understood and in use today, human germ-line manipulation, which would be required to add an allele back, remains much further in the future. Additionally, while it may be possible to re-select for an allele that had previously been actively selected against, it would take much longer for an allele to increase in frequency in a population than it did to decrease. These rates differ for the simple reason that you can only select for what is already present and many parents would not have the desired allele.

One additional eugenics-related concern is that of discrimination. Some bioethicists worry that if PGD for a particular condition became widespread, discrimination against those few remaining individuals with the condition would increase (Stock 2002). For instance, if PGD to eliminate Down syndrome was the norm, discrimination toward those few born with the ailment would potentially be worse than it was previously. This concern is simple to understand and may have some basis in reality, but it does not provide a reason to limit PGD usage. Attempting to eliminate or reduce the prevalence of a condition need not impact the respect with

which society treats those with the condition. By this reasoning we should logically restrain ourselves from vaccinating against measles or eliminating accidents that might lead to paraplegia to avoid discriminating against those few who slip through the safety net (Savulescu 2001).

These eugenics-related worries are hypothetical but seem significant enough to warrant some concern. Given that there is no consensus regarding these issues in the United States, it seems that, at the very least, caution should be in order before embarking on a program of widespread PGD.

Policy Options

Current Policies in the United States

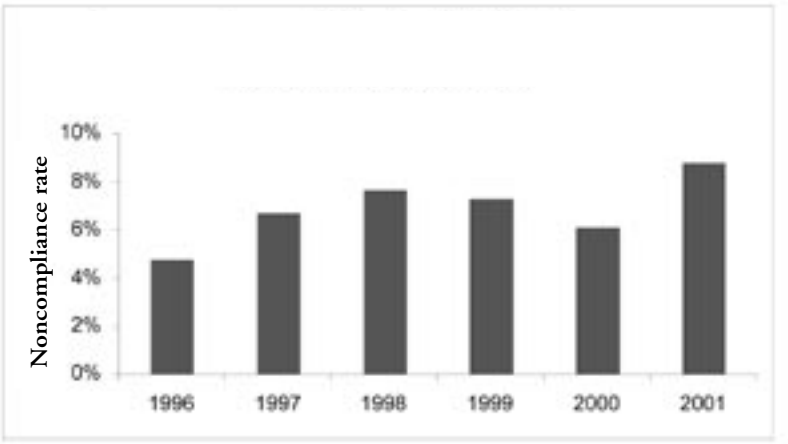
IVF was first performed in the United States in 1981, three years after the birth of Louise Brown in the United Kingdom (Jones et al. 1982). The technology was unregulated at that time, and the regulatory situation remains largely the same for all ART today with one exception. This exception is the Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA), which requires each ART program to annually report "pregnancy success rates achieved through each assisted reproductive technology" to the CDC (FCSRCA 1992). The CDC compiles the results of these reports each year into a publication that provides information for consumers regarding the success rates of each ART program.

These reports contain demographic data on parents who choose to use ART as well as success rates for the various technologies. The CDC considers five main technologies: IVF without ICSI, IVF with ICSI, gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT) and combinations of IVF with either GIFT or ZIFT. PGD is not considered an independent technology nor is it tracked in any way in the CDC data. The CDC contracts with the Society for Assisted Reproductive Technology (SART) to acquire the data for the annual report. SART is responsible for maintaining a master list of all ART programs in the United States and for contacting each program every year to request the necessary data.

To ensure the accuracy of the data published in the report, the CDC and SART have utilized a variety of approaches to verify the information provided by the ART programs. From 1994 to 1999, the CDC and SART visited a randomly selected subset of clinics and verified the data submitted by comparing it to the actual medical records. More recently, SART has used a self-verification process in which each program is asked to re-report detailed data on a randomly selected subset of ART treatment cycles. Both of these verification procedures indicated that the original data submitted was quite accurate. Furthermore, most discrepancies were related not to

the success or failure of IVF cycles but to details, such as the source of the original infertility or the use of specialized and rare procedures, such as GIFT or ZIFT. One concern with the self-reporting system recently used has been relatively low compliance among the ART programs, as only approximately 60 percent of clinics completed the verification process in 2000.

Figure 2: Percentage of Fertility Clinics Not Complying with the FCSRCA for Any Reason



Source: CDC annual ART reports, compiled by author.

Another concern with the FCSRCA is noncompliance with the act itself. Although all ART programs are required to participate, the act does not proscribe any penalties for noncompliance beyond the publication of the program's name as a non-complier. This has not proven to be a particularly effective deterrent as the CDC has reported noncompliance rates between 5 and 9 percent over the entire history of the program (Figure 2). With the exception of this persistent noncompliance, however, the FCSRCA seems to be a largely effective mechanism to provide the public with information on the use of ART and on the relative merits of the various ART programs.

Beyond the FCSRCA there is very little federal regulation of ART in the United States. Some programs fall under the Clinical Laboratories Improvement Amendments of 1988, which focus on quality control issues at clinical laboratories, but, as currently interpreted, the majority of fertility clinics are not covered by this legislation (Genetics and Public

Policy Center 2004). Additionally, the FDA has indicated its intention to regulate all "manufacturers" of "biological products." This regulation may include oversight of laboratories working with reproductive tissues in certain circumstances, but the extent to which the FDA's proposed rules would cover clinics performing IVF or similar procedures is still an open question (Genetics and Public Policy Center 2004).

Some states regulate ART as well, although for the most part states have not chosen to assume oversight responsibility for ART programs (Genetics and Public Policy Center 2004). Rather, most state laws focus on defining parentage or ensuring that appropriate informed consent is obtained prior to the transfer of embryos. At least fifteen states also have laws requiring some insurers to cover infertility treatment (Genetics and Public Policy Center 2004). Although these laws vary by state, most require certain insurers to offer coverage and let employers know that this coverage is available (INCIID 2003). They do not typically mandate that employers include the coverage in their employee insurance plans.

A Proposal for PGD Monitoring in the United States

Given the lack of consensus regarding the ethical acceptability of PGD and the possibility that the technology could grow in popularity quite substantially, the current absolute lack of regulation of the technology seems inappropriate. This dearth of regulation is not troubling because PGD seems to be a technology in dire need of regulation, but because it leaves both the public and the government almost totally in the dark regarding its use.

A simple solution to this shortage of information would be to require reporting by ART clinics regarding their use of PGD. Such a regulation would serve two purposes. First, similar to the FCSRCA, it would allow the public to see the success rates of PGD procedures at various programs around the country and thus serve as a valuable resource for couples considering PGD. Second, it would provide an important data point to both the public and the government regarding the extent of use of the technology. Ideally, to be useful, this reporting requirement should not only require clinics to report on the use of PGD but also on the particular genetic characteristic or characteristics selected for. This would allow interested parties to examine how PGD was used in practice and assess whether it was being used for medical or nonmedical purposes and whether it seemed likely to lead to unintended eugenic consequences.

As it is often easier to modify existing regulations than to start anew

in the United States, a promising approach to monitoring PGD would be to modify the FCSRCA. The Act gives the Secretary of Health and Human Services the right to include any specific technology he or she sees fit, subject to public comment. This clause suggests that the Department of Health and Human Services (DHHS) could add PGD without the need for any legislative action. This simple action would ensure the availability of data on the frequency of PGD's use and the success rates associated with such use.

Mandating the reporting of the specific genetic characteristics screened for in PGD procedures would require a more extensive modification of the FCSRCA and might require legislative action. Although passing new legislation, even to simply modify an existing law, would undoubtedly be complicated and time-consuming, the process could have other benefits. In particular, the new legislation could be crafted with stronger penalties for noncompliance, which could potentially reduce the persistent noncompliance that has plagued the current rule.

A logical approach to implementing this monitoring program would be for DHHS to add PGD to the FCSRCA first and then begin the lengthier process of proposing a legislative modification. This sequential approach would have the benefit of generating some initial data rapidly rather than waiting until complete data could be obtained.

Although some benefits of this policy seem clear, it is important to fully assess its consequences. Beyond the greater consumer information, which would facilitate comparisons between ART programs and increase general knowledge of society's use of PGD, there would almost certainly be other indirect consequences. It is possible to imagine a report that indicated reasonably widespread use of PGD encouraging other parents to use the technology themselves. This could occur, for instance, if parents thought their children would be disadvantaged if they failed to use PGD. In many cases, this tendency would likely have a homogenizing effect, but it is also possible that some parents would deliberately choose different traits in order to help ensure that their children were unique.

It is also conceivable that reporting on PGD could increase opposition to the technology. If a report indicated that selection against genes related to a particular skin color or sexual orientation was prevalent, it could create a significant uproar and perhaps even a backlash against the technology. It is possible that in such a situation enough of a consensus could be reached that the use of the technology in general would be regulated.

An interesting and potentially troubling consequence of reporting could be the hypothetical situation in which the government itself becomes

concerned with reported trends in PGD use. It is conceivable that a trait that gained popularity among parents could be considered undesirable by the government for one reason or another. However, given the strong sentiment against government interference in reproduction in the United States it seems essential that the government not be given any control over the use of PGD. Regulation of the use of PGD, were it to come later, would need to be initiated and strongly supported by private citizens for it to have any chance of success. Such a policy would be in agreement with the FCSRCA which states "the Secretary may not establish any regulation, standard, or requirement which has the effect of exercising supervision or control over the practice of medicine in assisted reproductive technology programs" (FCSRCA 1992).

Public reporting of PGD data would prevent the technology from continuing to develop without public scrutiny, and would allow the public and the government to quantify the use and growth of the technology. This information would help the public assess the impact of PGD and facilitate more stringent regulations of the technology should society eventually decide that such regulation is necessary.

Conclusion

Nearly fifteen years after its first use, PGD remains largely a fringe technology, but the potential power of the technique combined with ongoing technical progress suggest that its use could grow substantially in the future. Were PGD to become sufficiently prevalent, it would have a far-reaching impact on society, yet there is little consensus on the nature of this impact or on its desirability. Given this uncertainty, the status quo in which PGD develops and gains in popularity outside the realm of public scrutiny is not in society's best interest. Rather, the government should, as it has with IVF, mandate basic public reporting of the use of PGD. Such a policy would provide the American people with the information they need to monitor the growth of the technology and help them to make a thoughtful and reasoned decision on the use of PGD.

Notes

[1] The author would like to thank Harold T. Shapiro for helpful comments and suggestions on an earlier draft of this paper. This work was funded in part by a National Science Foundation Graduate Research Fellowship.

References

Braude, P., S. Pickering, et al. 2002. Preimplantation Genetic Diagnosis. *Nature Reviews Genetics* 3(12): 941-53.

Braude, P. and P. Rowell. 2003. Assisted Conception II: In Vitro Fertilisation and Intracytoplasmic Sperm Injection. *British Medical Journal* 327(7419): 852-855.

Critser, J. K. 1998. Current Status of Semen Banking in the USA. *Human Reproduction* 13 Suppl 2: 55-67; discussion 68-9.

Daniels, N. Is There a Right to Health Care and, if so, What Does it Encompass? In Kuhse, H. and P. Singer. *A Companion to Bioethics*. Oxford: Blackwell Publishers.

ESHRE PGD Consortium Steering Committee. 2002. ESHRE Preimplantation Genetic Diagnosis Consortium: Data Collection III (May 2001). *Human Reproduction* 17(1): 233-46.

Fertility Clinic Success Rate and Certification Act of 1992 (FCSRCA). 1992. *U.S. Code* 42, 263a-1 et seq (Public Law 102-493).

Gardner, D. K., M. Lane, et al. 2000. Culture and Transfer of Viable Blastocysts: A Feasible Proposition for Human IVF. *Human Reproduction* 15 Suppl 6: 9-23.

Genetics and Public Policy Center. 2002. Public Awareness and Attitudes about Reproductive Genetic Technology. Genetics and Public Policy Center, Johns Hopkins University, Washington, DC. http://dnapolicy-content.labvelocity.com/pdfs/4/27374.pdf (accessed March 10, 2005).

_____. 2004. Preimplantation Genetic Diagnosis: A Discussion of Challenges, Concerns, and Preliminary Policy Options Related to the Genetic Testing of Human Embryos. Genetics and Public Policy Center, Johns Hopkins University, Washington, DC. http://dnapolicy.stage.labvelocity.com/downloads/pdfs/policy_pgd.pdf (accessed March 10, 2005).

Handyside, A. H., J. G. Lesko, et al. 1992. Birth of a Normal Girl after In Vitro Fertilization and Preimplantation Diagnostic Testing for Cystic Fibrosis. *New England Journal of Medicine* 327(13): 905-9.

Human Fertilisation and Embryology Authority (HFEA). 2002. Patients' Guide to IVF Clinics. London, United Kingdom. http://www.hfea.gov.uk/ForPatients/PatientsGuidetoIVFClinics (accessed March 10, 2005).

InterNational Council on Infertility Information Dissemination (INCIID). 2003. *States Mandating Insurance Coverage for Infertility and Pregnancy Loss*. http://www.inciid.org/printpage.php?cat=insurance101&id=15 (accessed March 10, 2005).

International Human Genome Sequencing Consortium. 2004. Finishing the Euchromatic Sequence of the Human Genome. *Nature* 431(7011): 931-45.

Jones, H. W., Jr., G. S. Jones, et al. 1982. The Program for In Vitro Fertilization at Norfolk. *Fertility and Sterility* 38(1): 14-21.

Kass, L. 2002. *Life, Liberty and the Defense of Dignity*. San Francisco: Encounter Books.

Kitcher, P. 2003. Utopian Eugenics and Social Inequality. In *Mendel's Mirror: Philosophical Reflections on Biology*. New York: Oxford University Press.

Melie, N. A., O. A. Adeniyi, et al. 2003. Predictive Value of the Number of Oocytes Retrieved at Ultrasound-Directed Follicular Aspiration with regard to Fertilization Rates and Pregnancy Outcome in Intracytoplasmic Sperm Injection Treatment Cycles. *Fertility and Sterility* 80(6): 1376-1379.

Paul, D. B. 1995. *Controlling Human Heredity: 1865 to the Present*. Atlantic Highlands, NJ: Humanities Press.

Pence, G. 2000. Maximize Parental Choice. In Stock, G. and J.Campbell, *Engineering the Human Germline*. New York: Oxford University Press.

Savulescu, J. 2001. Procreative Beneficence: Why We Should Select the Best Children. *Bioethics* 15(5-6): 413-26.

Sermon, K. 2002. Current Concepts in Preimplantation Genetic Diagnosis (PGD): A Molecular Biologist's View. *Human Reproduction Update* 8(1): 11-20.

Silver, L. 1997. *Remaking Eden*. New York: Avon.

Steckel R.H. 1995. Stature and the Standard of Living. *Journal of Economic Literature* 33(4): 1903-1941.

Steptoe, P. C. and R. G. Edwards. 1978. Birth after the Reimplantation of a Human Embryo. *Lancet* 2(8085): 366.

Stock, G. 2002. *Redesigning Humans*. New York: Houghton Mifflin.

U.K. Department of Health. 2002. Preimplantation Genetic Diagnosis (PGD): Guiding Principles for Commissioners of NHS Services. http://www.dh.gov.uk/assetRoot/04/01/92/44/04019244.pdf (accessed March 10, 2005).

U.K Office of National Statistics. 2003. *Live Births*. http://www.statistics.gov.uk/cci/nugget_print.asp?ID=369 (accessed March 10, 2005).

U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. 2003. *2001 Assisted Reproductive Technology Success Rates*. U.S. Department of Health and Human Services.

Wright, V. C., L. A. Schieve, et al. 2003. Assisted Reproductive Technology Surveillance: United States, 2000. *Morbidity and Mortality Weekly Report - Surveillance Summaries*